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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,080	09/24/2008	Mervi Ahlroth	GJE-7664	9433

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SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO Box 142950
GAINESVILLE, FL 32614

EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
07/01/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/586,080	AHLROTH ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 8-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 May 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed an amendment to the claims. Claim 6 is amended. Claims 15-18 are new.

Election/Restrictions

Applicant's election without traverse of Group 2 in the reply filed on March 22, 2010 is acknowledged.

Claims 1-5, 8-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 22, 2010.

Claims 6, 7, 15-18, drawn to a fusion protein comprising an endonuclease fused to an integrase, are under consideration.

Information Disclosure Statement

Applicant filed an Information Disclosure Statement (IDS) on August 4, 2008. The IDS has been considered.

Specification

The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is

on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

Figures 5 and 6 are drawn to nucleotide sequences. SEQ ID NOs. must be assigned to these sequences. The sequences must also be provided in computer readable format (CRF) and on paper and a statement indicating sequences on the CRF and on paper are the same must also be included.

Appropriate correction is required.

The absence of proper sequence listing did not preclude the examination on the merits however, **for a complete response to this office action, applicant must submit the required material for sequence compliance.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 7, 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bushman, WO 95/32225, published November 30, 1995, see IDS, Manino et al., 1999, Biochemistry, 38: 16189-16186, see IDS, Dujon et al., US Patent 5,474,896, patented December 12, 1995.

Bushman teaches that retroviral vectors are a popular means for delivering DNA in gene therapy protocols. However, insertion of retroviral DNA can result in inactivation

or ectopic activation of cellular gene, thereby causing diseases. Thus, methods for site-specifically controlling the location of integration of retroviral vectors are desired to overcome this problem (Bushman, page 2, 5th parag. to page 3, 2nd parag.). Bushman teaches that the chimeric protein comprises a "first domain" that attaches the chimeric protein to target nucleic acid and a "second domain" that integrates donor nucleic acid into the target nucleic acid. The first domain can be either a "DNA-binding domain" or a "protein-binding domain" that is operative to couple and/or associate the chimeric protein with a recognition sequence on the target nucleic acid. DNA-binding domains are typically derived from DNA binding proteins and are found in proteins including transcription control proteins, recombination enzymes, and DNA-modifying enzymes. DNA-modifying enzymes include restriction enzymes, DNA-repair enzymes, site-specific methylases, and the like. The second domain functions to promote integration of donor nucleic acid into target nucleic acid. Typically, the second domain is derived from an integrase protein. One preferred integrase protein is a retroviral integrase, which includes HIV-1 (Bushman, pages 6-12; more specifically, see page 6, parag. 1-3 under Detailed Description of the Invention, page 9, 3rd parag., page 10, 3rd parag. to page 11).

While Bushman teaches making chimeric proteins comprising a DNA binding domain and an integrase, wherein the DNA binding domain can be obtained from a restriction enzyme and wherein the integrase can be obtained from a retrovirus, including that of HIV-1, Bushman does not teach using restriction enzymes PpoI, CreI, and H98A.

At the time of filing, Mannino et al. teach that homing endonucleases, like type II bacterial restriction endonucleases, catalyze the hydrolytic cleavage of DNA in a site-specific manner. However, the recognition sequences of homing endonucleases are, in general, substantially longer than are those of restriction endonuceases. Recognition sequence of homing endonucleases range from 15 to 40 base pairs and these enzymes show degeneracy in the recognition of these target sites that resembles the degeneracy of transcription factors (Manino et al., page 16178, 1st col., 1st parag.). PpoI and its mutant, H98A, are two examples of homing endonucleases (Manino et al., page 16179, 1st col. under Production of I-PpoI Endonuclease in Escherichia coli). It is noted that an artisan would have used a homing endonuclease because longer recognition sites in the genome are rarer than recognition sites that restriction endonucleases bind. This means that a smaller number or sites are recognized in the genome by homing endonucleases than restriction endonucleases and would also mean that fewer sites in the genome are cut by the homing endonuclease fused to an integrase. This would address Bushman's issue that one problem with integrases is that it inserts in the genome, sometimes hitting critical genes. Using an endonuclease that has a small number of potential sites to integrate would reduce the probability that the endonuclease-integrase fusion protein of hitting a critical gene.

With regard to using CreI (claim 16), the art teaches that CreI is also a homing endonuclease (Dujon et al., col. 10, first table) and an artisan would have used CreI because it is a functional equivalent with regard to being an endonuclease that recognizes a long nucleotide sequence.

With regard to the claims being drawn to the endonuclease being specific to a site in an abundant rDNA locus (claim 6), it is noted that this is an inherent property of homing endonucleases. For example, Makino et al. teach that PpoI cleaves recipient rDNA at the site of intron integration (Makino et al., page 16178, 1st col., 2nd parag. to 2nd col.).

Thus, the claims are rejected.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

(EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Joanne Hama/
Primary Examiner
Art Unit 1632

Application No.: 10/586,080

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

[X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

[ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

[ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

[ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing".

[ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

[ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the
"Sequence Listing" as required by 37 C.F.R. 1.821(e).

[ ] 7. Other:

Applicant Must Provide:

[X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing". (If the unidentified sequences are not provided on the CRF)

[X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification. (If the unidentified sequences are not provided in the paper copy)

[X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). (If a new paper and/or CRF are required)

For questions regarding compliance to these requirements, please contact:

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